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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,522	04/16/2004	Geert Plaetinck	D0590.70011US02	2890
23628 7590 06/29/2010 WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206				
EXAMINER SHIN, DANA H				
ART UNIT		PAPER NUMBER		
1635				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/826,522

Applicant(s)

PLAETINCK ET AL.

Examiner

DANA SHIN

Art Unit

1635

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-41, 70-74 and 80-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30-41, 70-74 and 80-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB-06)
Paper No(s)/Mail Date 4-7-2010
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on April 7, 2010.

Currently, claims 30-41, 70-74, and 80-83 are pending and under examination on the merits in the instant case.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Objections/Rejections

Priority

The denial of granting the foreign priority date for claim 34 remains effective for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has dismissed the priority objection and failed to properly address this objection. Hence, the foreign priority denial is maintained.

Claim Rejections - 35 USC § 102

Claims 30-36, 39, 74, 80, and 83 remain rejected under 35 U.S.C. 102(e) as being anticipated by Graham for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant's arguments filed on April 7, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not anticipated because Graham does not teach that "one copy of a gene sequence is placed between two promoters and that this one copy of the gene sequence is a template for both the sense and antisense transcript." Contrary to applicant's argument, Graham's construct meets every structural limitation for the expression vector claimed in the instant case. The claimed expression vector, which is contained in a micro-organism, comprises two promoters that flank a DNA sequence, wherein the two promoters transcribe and produce a double-stranded RNA product in the micro-organism. Now, as noted in the last Office action, Graham teaches a yeast cell or a bacterial cell comprising an expression vector that represses the expression of a target gene when introduced into an animal cell. Graham teaches that the expression vector contains two copies of DNA sequence, each being placed under a promoter that is suitable and operable in the cell such that one copy is placed in the sense orientation under one promoter and the other copy is placed in the antisense orientation under another promoter, wherein one of the copies is substantially identical to a region of a target gene. Although Graham discloses "two copies" of a structural gene sequence within the construct, wherein "one copy" of the structural gene sequence is in the sense orientation and "the other copy" of the structural gene sequence is in the antisense orientation, the word "two copies" does not indicate that the sense orientation copy and the antisense orientation copy are *not* contiguous so as to form a single, one DNA "sequence". That is, there is nothing in the disclosure of

Graham that teaches that the construct of Graham is exclusively limited to two separate DNA “sequences”. That is, the construct of Graham encompasses the following structure in the 5’ to 3’ direction in a contiguous manner: one promoter-“one copy” of the structural gene sequence in the “sense orientation”-“the other copy” of the structural gene sequence in the “antisense orientation”-another promoter, wherein “each copy of said structural gene sequence is separately placed under the control of a promoter”. As such, the “two copies” of the structural gene sequence form a single, one DNA sequence flanked by one promoter at the 5’ end and another promoter at the 3’ end as claimed in the instant case.

Applicant argument that Graham teaches the use of two different promoters in different embodiments. It is found that applicant's argument is moot because no claim in the instant case is directed to a micro-organism having two different promoters.

Since applicant's arguments are not persuasive, this rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 30-41, 70-74, and 80-83 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Timmons et al., McAllister et al., Conkling et al., and Talkad et al. for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant's arguments filed on April 7, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not obvious because the combination of the references does not teach all of the elements of the claims. In particular, applicant only focuses on a single reference, the McAllister et al. reference, and argues that the reference teaches a DNA vector that transcribes RNA transcripts “complementary to either strand” or “either one” of

a DNA sequence. Contrary to applicant's argument that the vector system of McAllister et al. is different from the construct claimed in the instant case, the DNA vector of McAllister et al. that is capable of "transcription of DNA to produce RNA strands complementary to either one of the strands of the inserted DNA sequence", "wherein transcription from either of the phage promoters proceeds toward the other promoter and in a direction opposite from the direction of transcription of the other phage promoter" (emphasis added). See claim 7. As such, the vector system of McAllister et al. is capable of transcribing "both" RNA "strands" that are complementary to the "strands" of the single DNA "sequence". That is, as claimed, the vector system of McAllister et al. can produce the sense orientation DNA sequence and at the same can produce the antisense ("a direction opposite from the direction of transcription of the other phage promoter") orientation DNA sequence, thereby being capable of simultaneously transcribing both RNA "strands" of the inserted DNA sequence. Again, in no way is the vector system of McAllister et al. is limited to a vector that produces only one RNA "strand" of the inserted DNA sequence when the DNA sequence is flanked by two promoters in opposite direction and the transcription from the two promoters proceeds in opposite directions.

Applicant further asserts that the claims are not obvious by treating the vector system of McAllister et al. as same as that of Noren et al. (US 5,691,140), which is no longer cited in the obviousness rejections pending in the instant case. Applicant then points out the declaration of Erwin Sablon submitted for Application No. 10/057,108 and argues that the vector of Noren et al. "ensures that only one strand was transcribed," and therefore concludes that "McAllister fails to describe an element of the claimed invention, and none of the other cited reference provide this missing element." Applicant's attention is directed to the fact that there is no evidence establishing that the vector of Noren et al. is identical to or same as that of McAllister et al. such

that both vectors are designed to ensure that only one strand is transcribed as declared by Erwin Sablon for the Noren et al. reference. For example, Erwin Sablon declared that the vector of Noren et al. is not intended to produce two RNA strands because its purpose is “to generate highly specific RNA probes”, and therefore “it is crucial that only one strand becomes transcribed”. See paragraph 9. In the instant case, however, there is no evidence showing that the purpose of the vector of McAllister et al. is only to generate RNA probes. As such, one cannot establish the same rationale used for the Noren et al.’s vector such that “it is crucial that only one strand becomes transcribed”. Hence, it is improper to apply the declaratory statements specific for a different prior art reference (the Noren et al. US Patent) that is not included in the instant rejection to support applicant’s asserted nonobviousness of the claims.

Applicant further argues that the claims are not obvious because there is no motivation to introduce the vector of McAllister et al. into the organisms of Timmons et al. or to modify the vector of Timmons et al. Contrary to applicant’s argument, one of ordinary skill in the art would have been motivated to modify the dsRNA-producing vector of Timmons et al. by replacing the muscle tissue-specific promoter at the 5’ end with art-recognized bacteriophage promoters at the 5’ end and the 3’ end of the DNA sequence that produces a dsRNA, because it was known in the art that one can express a dsRNA in *C. elegans* by feeding bacteria containing or expressing the dsRNA (see Timmons et al.) and because it was known that bacteriophage promoters are capable of transcribing an inserted DNA sequence and produce RNA strands within bacteria. Hence, one would have been sufficiently motivated to make a bacteria-expressionable vector using bacteriophage promoters. Further, contrary to applicant’s argument that one has no motivation to use the vector system of McAllister et al. because it produces only “single stranded RNA probes.”, it is noted that there is no objective evidence showing that the vector of McAllister et

al. is only limited to generating single-stranded RNA probes. In addition, the vector system of McAllister et al. is capable of transcribing both RNA strands of the inserted DNA sequence, one strand in the sense orientation and the other stand in the antisense orientation as explained on page 5 of this Office action. Hence, one would have been motivated to use the vector system of McAllister et al. in order to transcribe or express a double-stranded RNA in a micro-organism.

Since applicant's arguments are not persuasive, this rejection is maintained.

Claims 30-41, 70-74, and 80-83 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al., Graham, Ely et al., and Talkad et al. for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant's arguments filed on April 7, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not obvious because the Fire et al. provisional application (e.g., claims 1, 14, 16, 20 of 60/068,562) does not provide adequate written description for the claimed subject matter. In particular, applicant asserts that since claims 14, 16, and 20 each depends from claims 1-21, the "claims fail to teach their individual recitations in combination with anything other than the recitations of claims 1-12." First, applicant's attention is directed to the fact that the instant rejection is not an anticipation rejection wherein a single reference (Fire et al.) teaches all of the limitations. Rather, the instant rejection is an obviousness rejection that requires only a reasonable expectation of success, not absolute predictability of success. See *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988) at 1681. Second, applicant's attention is directed to the fact that claims 1, 14, 16, and 20 are not the only disclosure of 60/068,562. As noted in the last Office action, the entirety of the 60/068,562 application including for example claims 1, 14, 16, and 20 and pages 11 and 13 provides

adequate support description for a target inhibition method in *C. elegans* with an expression vector that synthesizes two separate complementary RNA strands that form an RNA duplex, wherein the synthesis of the two RNA strands is driven by bacteriophage polymerase promoters such as T3, T7, and SP6 promoters.

Applicant argues that "based on the knowledge in the art at that time, as evidenced by the Sablon Declaration that is described above, the skilled person would not have even attempted to make this combination." As noted hereinabove, the declaration of Erwin Sablon discusses a very specific type of vector disclosed in the Noren et al. reference that is not cited in the instant rejection. Further, it is found that the declaration also discusses the Zdinak et al. reference. Hence, the declarant concludes that "based on the cited prior art references", one would not have had a reasonable expectation of success (emphasis added). See paragraph 17. Note that the "cited" prior art references stated in the declaration is different from the cited prior art references in the instant rejection. In particular, note that neither the Noren et al. reference nor the Zdinak et al. reference discussed in the declaration is cited in the instant rejection. Taken together, the declaration of Erwin Sablon does not provide any objective reason to doubt the knowledge in the art based on the prior art references cited in the "instant" rejection would have prevented one from attempting the claimed subject matter or arriving at the claimed subject matter.

Applicant continues to argue for the nonobviousness of the claims by attacking the Fire et al. reference and states that the vectors of Fire et al. cannot be used to produce a double-stranded RNA. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the provisional application of the Fire et al. reference does not provide adequate written description for the WO document and therefore the WO document is not prior art. Contrary to applicant's argument, the entirety of 60/068,562 provides adequate written description for a target inhibition method in *C. elegans* with an expression vector that synthesizes two separate complementary RNA strands that form an RNA duplex, wherein the synthesis of the two RNA strands is driven by bacteriophage polymerase promoters such as T3, T7, and SP6 promoters, which is also taught in the WO document. Hence, the Fire et al. WO document is a proper prior art reference.

Applicant argues that the claims are not obvious because Graham does not teach an element of the claimed invention ("only one structural gene sequence"). Contrary to applicant's argument, the word "copy" or "copies" used in the Graham reference is not synonymous with the word "sequence", nor does the word indicate that the two copies comprising the sense "sequence" and the antisense "sequence" are not contiguous. That is, as noted at page 5 hereinabove, the vector structure of Graham reference fully reads on a DNA vector having the following elements from 5' to 3' direction: one promoter-sense strand copy of a structural gene DNA "sequence"-antisense strand copy of a structural gene DNA "sequence"-another promoter in opposite orientation, thereby forming "each" copy being separately placed under the control of one promoter, and also forming a single DNA "sequence" flanked by two promoters that are placed in opposing or opposite directions. Hence, Graham teaches the allegedly missing "element of the claimed invention."

Applicant argues that the claims are not obvious because the "motivation" stated on page 10 of the last Office action is incorrect as the vectors of Fire et al. and Graham are not "art-recognized equivalents" as the citations in the Fire provisional applications relate to "standard"

laboratory manuals whereas the vector of Graham is "novel" as it is a patented invention. It appears that applicant has mischaracterized and misunderstood the concept of "art-recognized equivalents". The concept of the term "art-recognized equivalents" used in MPEP 2144.06 refers to "functional or mechanical equivalents". As such, the determination as to whether the vector of Fire et al. and that of Graham are "art-recognized equivalents" depends on whether the vectors are "functional" or "mechanical" equivalents such that one can substitute for the other, and it does not depend on whether one vector is made by using "standard laboratory manuals" and the other is made by novel means. The vector of Fire et al. that produces a double-stranded RNA by using a bacteriophage promoter is "functionally" equivalent to the vector of Graham that produces two RNA strands from two bacteriophage promoters that are placed in opposite directions. Further, from the perspective that both vectors utilize a bacteriophage promoter or promoters to synthesize and express an RNA molecule in a cell, the two vectors are also "mechanically" equivalent.

Since applicant's arguments are not persuasive, this rejection is maintained.

Double Patenting

Claims 30-41, 70-74, and 80-83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 8-11 of 11/522,307 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has not provided any rebuttal argument because applicant has failed to address the supposed errors of this rejection, nor has applicant submitted a signed terminal disclaimer. Hence, this rejection is maintained.

Claims 30-41, 70-74, and 80-83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 24-25 of 11/666,017 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has not provided any rebuttal argument because applicant has failed to address the supposed errors of this rejection, nor has applicant submitted a signed terminal disclaimer. Hence, this rejection is maintained.

Claims 30-41, 70-74, and 80-83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 27-28 and 34-35 of 11/666,021 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has not provided any rebuttal argument because applicant has failed to address the supposed errors of this rejection, nor has applicant submitted a signed terminal disclaimer. Hence, this rejection is maintained.

Claims 30-41, 70-74, 80, and 83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 34-39 of 12/055,607 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has not provided any rebuttal argument because applicant has failed to address the supposed errors of this rejection, nor has applicant submitted a signed terminal disclaimer. Hence, this rejection is maintained.

Claims 30-41, 70-74, 80, and 83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 6-10 and 12 of 12/087,537 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant has not provided any rebuttal argument because applicant has failed to address the supposed errors of this rejection, nor has applicant submitted a signed terminal disclaimer. Hence, this rejection is maintained.

Claims 30-41, 70-74, 80, and 83 remain rejected on the ground of nonstatutory obviousness-type double patenting over claims 26-27 of U.S. Patent No. 7,358,069 B2 for the reasons of record as set forth in the Office action mailed on December 7, 2009 and for the reasons stated below.

Applicant's arguments filed on April 7, 2010 have been fully considered but they are not persuasive. Applicant argues that the instant claims are not obvious over the reference claims of 7,358,069 B2 because the instant claims do not recite "a terminator linked to a promoter. Thus the claims are patentably distinct". Contrary to applicant's argument, the instant claims are obvious over the reference claims because the expression vector of the instant claims do not exclude "a terminator linked to a promoter" as the claims explicitly recite the open-ended transitional term "comprises" for the expression vector and therefore do not exclude any unrecited elements. See the phrase: "A micro-organism, comprising an expression vector that comprises" in lines 1-2 of claim 30 of the instant application. As such, the expression vector of the instant claims does not exclude a transcription terminator operably linked to a promoter as further evidenced by the fact that an expression vector contains or comprises a polyadenylation

signal sequence (terminator) operably linked to a promoter. See page 3 of the instant specification that specifically teaches that the claimed expression vector comprises a nucleotide sequence encoding stop codons. Hence, the instant claims and the reference claims are obvious variants of each other and thus are not patentably distinct from each other. Accordingly, this rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi (Acting SPE) can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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